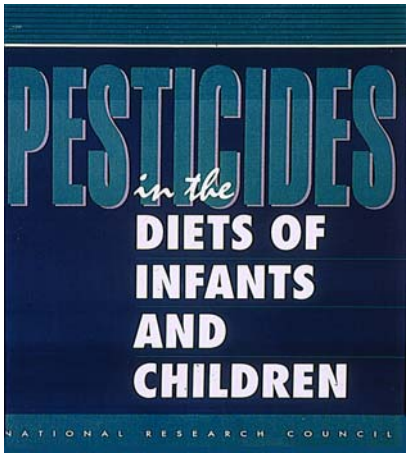
NIEHS and Children's Environmental Health

Philip J. Landrigan, MD, MSc, FAAP
Professor of Pediatrics
Professor and Chairman
Department of Community & Preventive Medicine
Mount Sinai School of Medicine

The Beginning of the Modern Era in CEH Research - June 1993



- ***Children are not little adults***
- ***Proportionately greater exposures***
- ***Unique windows of vulnerability***
- ***Early origins of adult disease***

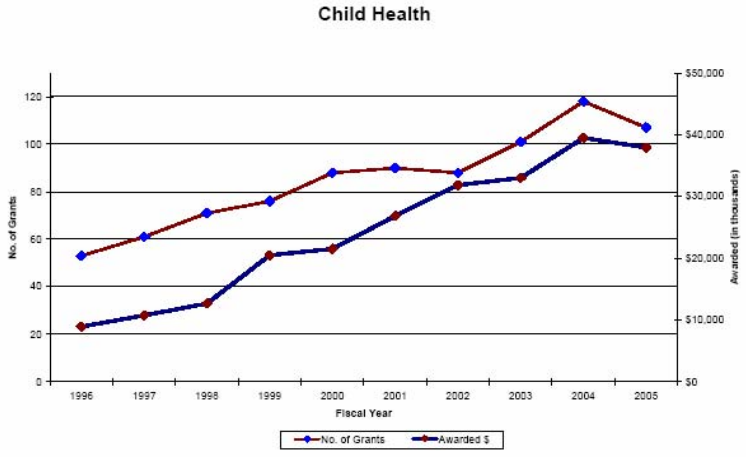
Consequences of the NAS Report

Passage of the Food Quality Protection Act – 1996 (by unanimous vote of both houses of Congress)

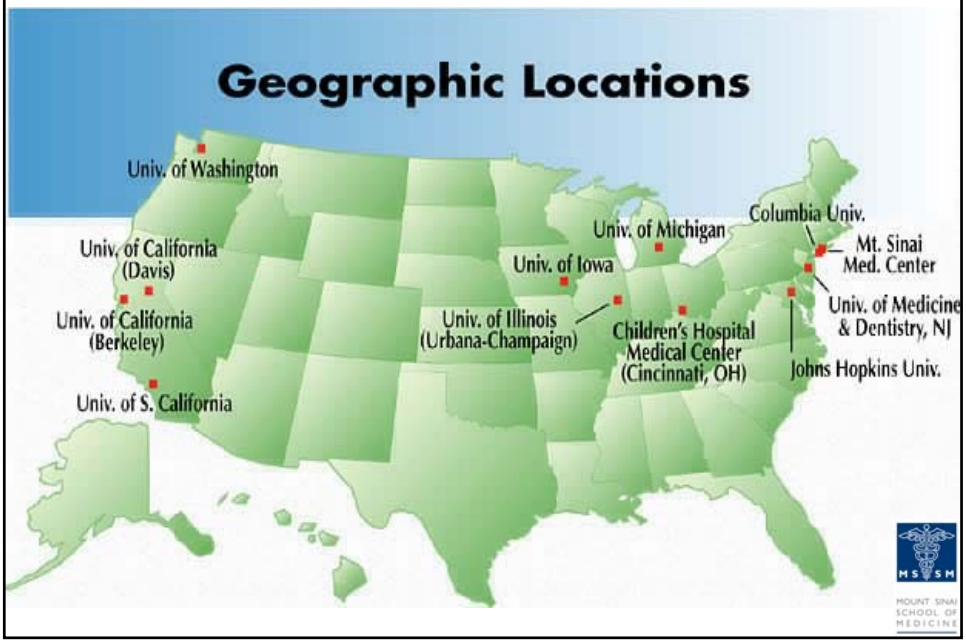
- Creation of EPA's Office of Children's Health Protection
- Presidential Executive Order on Children's Environmental Health and Safety
- National network of CEH research centers
- Pediatric Environmental Health Specialty Units
- The National Children's Study

NIEHS
National Institute of Environmental Health Sciences

Ten Year History of Funding of Children's Environmental Health Grants



CEH Centers in the USA



Scientific Challenges and Opportunities

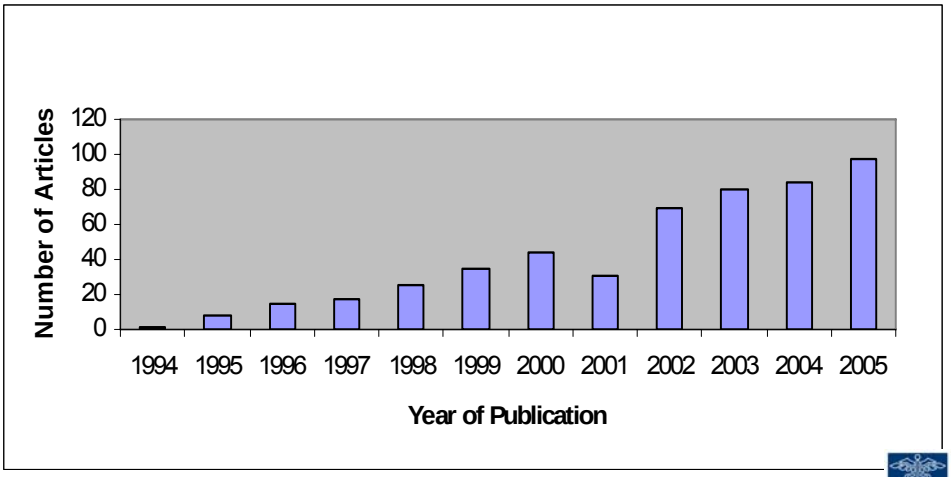
Basic Biology → Integrative → Clinical → Public Health

Complex Diseases of Childhood and Beyond

- **Asthma**
- **Autism, ADHD and other neurobevioral disorders**
- **Childhood cancers**
- **Testicular cancer**
- **Certain birth defects –e.g., hypospadias**

- **Early origins of neurodegenerative diseases – dementia and PD**

Children's Environmental Health Reports, *EHP* – 1994-2005



Scientific Accomplishments

OPs & Neurobehavioral Disorders

Basic Biology Integrative Clinical Public Health

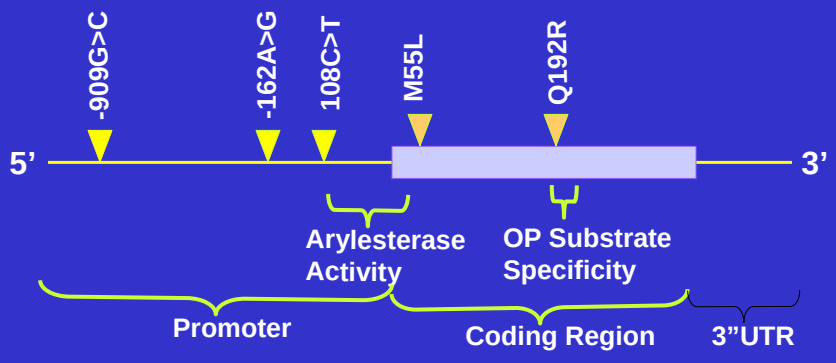
- **OP insecticides and brain development**
- **PON studies**

Scientific Accomplishments

OPs & Neurobehavioral Disorders - Biology

- **Slotkin et al. Developmental toxicity of CP – Inhibition of DNA synthesis in PC12 and C6 cells. *EHP* 2001; 109:909-13.**
- **Chen et al. Influence of genetic variation on PON1 activity in neonates. *EHP* 2003: 111:A591**
- **Mense et al Chlorpyrifos alters gene expression in human astrocytes. *Toxicol Science* 2006. 93: e125-35**

PON1 POLYMORPHISMS



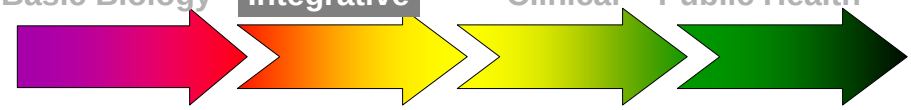
(Not drawn to scale; Introns omitted)

Chen et al., EHP 2003

Scientific Accomplishments

OPs &Neurobehavioral Disorders

Basic Biology | **Integrative** | Clinical | Public Health



- **New exposure assessment strategies**
- **New Biomarkers**
- **New diagnostic tests**

Scientific Accomplishments

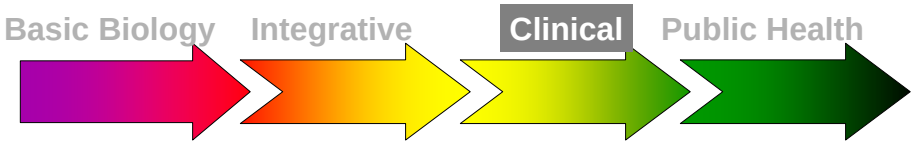
Ops & Neurobehavioral Disorders-Integrative

- **Fenske et al. Critical sampling and analytical issues for assessing children's exposures to pesticides. *EHP* 2005; 113:1455-62.**
- **Bradman A & Whyatt R. Methods for characterizing exposures to nonpersistent pesticides during pregnancy. *EHP* 2005; 113:1092-99.**
- **Whyatt et al. Biomarkers for assessing pesticide exposure during pregnancy. Toxicol Appl Pharm 2005; 206: 246-54.**

Examples: Dialkyl phosphates in urine; chlorpyrifos in blood; malathion dialkyl phosphate in urine.

Scientific Accomplishments

Ops & Neurobehavioral Disorders



- **Prenatal OP exposure and neonatal milestone delays**
- **Prenatal OP exposures and cognitive deficits**
- **Prenatal OP exposure, Attention Deficit Disorder (ADD) and Pervasive Developmental Delay (PDD)**

Scientific Accomplishments

Ops & Neurobehavioral Disorders – Clinical


PEDIATRICS

•**Rauh V et al. Impact of prenatal CP exposure on neurodevelopment in the first 3 years of life. *Pediatrics* 2006; 118: e1845-59**

Scientific Accomplishments

Ops & Neurobehavioral Disorders – Clinical

•Wolff, Eskenazi, Whyatt et al. Environmental exposures and birth outcomes in the NIEHS/EPA Children's Center birth cohorts. *Epidemiology* 2006. 17: S419-20

NEURODEVELOPMENT & OP EXPOSURE

	Brazelton	Bayley MDI	Bayley PDI	CBCL
Berkeley	↑ Reflexes DE, DM > older	↓ 24 m	=	↑ PDD = ATT ADHD 24 m
Mount Sinai	↑ Reflexes DE > older	↓ 24 m	=	
Columbia		↓ 36 m (NS 24m)	↓ 36 m (NS 24 m)	↑ PDD ↑ ATT ↑ ADHD 36 m

Scientific Accomplishments

OPs & Neurobehavioral Disorders

Basic Biology → Integrative → Clinical → **Public Health**

- **Ban on residential uses of CP and DZ**
- **Community intervention for IPM**

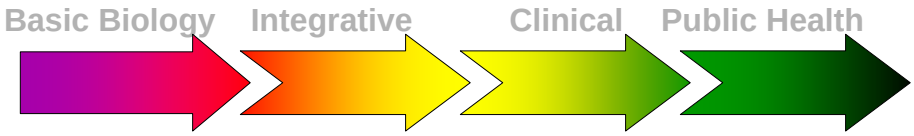
Scientific Accomplishments

OPs & Neurobehavioral Disorders-Public Health

- **Whyatt et al. Disappearance of CP effects on infant development after imposition of EPA ban on residential CP. *EHP* 2004; 112: 1125-32.**
- **Brenner B et al. Successful introduction of IPM in an inner-city community. *EHP* 2003; 111: 1649-53.**

Scientific Accomplishments -

OPs & Neurobehavioral Disorders



- OP insecticides and brain development
- PON studies

- New exposure assessment strategies
- New biomarkers
- New diagnostic tests

- Prenatal OP exposure and neonatal milestone delays
- Prenatal OP exposures and cognitive deficits
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- Ban on residential uses of CP and DZ
- Community intervention for IPM

Neurobehavioral Disorders

Future Challenges

Grandjean et al. *Lancet* 2006.
Developmental Toxicity of Industrial Chemicals – A Silent Pandemic

- 80,000 + industrial chemicals
- Developmental toxicology data available on only 200
- Human NDT data available for fewer than 10
- Almost no information available on toxicity of mixtures
- Urgent need for new strategies at every level of the 4-fold Schwartz paradigm
- New series in *Lancet*

Goals of this Workshop

To assist NIEHS to develop new strategies for maximizing the effectiveness of research in CEH – specifically, how to:

- Best advance etiologic research on the contribution of the environment to disease and dysfunction in children
- Best develop exposure and effects monitoring, epidemiology, clinical medicine and multidisciplinary studies
- Best develop novel strategies for intervention and prevention
- Best translate research findings to clinical and public health practice

These goals will be accomplished by considering 4 cases and deriving lessons from each.

MOUNT SINAI SCHOOL OF MEDICINE